AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. **(withdrawn):** A set of genetic polymorphisms being associated with optic neuropathy, which comprises at least one polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

2. (currently amended): A method for diagnosing or predicting susceptibility to open angle glaucoma in a human subject, comprising the steps of:

i) obtaining a biological sample from the subject,

ii) analyzing said sample to determine the nucleotide at position 462 of the Noelin 2 gene, and the nucleotide at position 1105 of the Myocilin gene, of said subject;

iii) making a diagnosis that said ~~patient~~ subject has, or is susceptible to, open angle glaucoma when said subject has at least one polymorphism selected from the group consisting of an adenine at position 462 of the Noelin 2 gene and a cytosine at position 1105 of the Myocilin gene.

3. (canceled).

4. (previously presented): The method of Claim 2, wherein said method further comprises analyzing said sample for the presence of at least one other genetic polymorphism associated with open angle glaucoma.

5-10. (canceled).

11. (withdrawn): A method for diagnosing or predicting susceptibility to Leber's disease in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of the set of the polymorphisms comprising at least one polymorphism selected from the group consisting of:

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro); and

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His), and

iii) diagnosing or predicting susceptibility to Leber's disease in the subject based on the genotype.

12. (withdrawn): The method of Claim 11, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

13. (previously presented): The method of Claim 2, wherein the nucleotide at position 462 of the Noelin 2 gene, and the nucleotide at position 1105 of the Myocilin gene, of said subject is determined by at least one technique selected from the group consisting of polymerase chain reaction (PCR), restriction fragment length polymorphism (PCR-RFLP) analysis, polymerase chain reaction followed by single strand conformation polymorphism (PCR-SSCP) analysis, ASO hybridization analysis, direct sequencing analysis, ARMS analysis, DGGE analysis, RNseA cleaving analysis, chemical restriction analysis, DPL analysis, TaqMan® PCR analysis, Invader® assay, MALDI-TOF/MS analysis, TDI analysis, single nucleotide extension assay, WAVE assay and a molecular fluorescent detection assay.

14. (withdrawn): A kit for diagnosing or predicting susceptibility to optic neuropathy in a human subject which comprises primer set and/or probe suitable for determining

genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

15. (withdrawn): The kit of Claim 14, wherein the optic neuropathy is glaucoma or Leber's disease.

16. (withdrawn): The kit of Claim 14, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

17. (withdrawn): A kit for diagnosing or predicting susceptibility to glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

18. (withdrawn): The kit of Claim 17, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

19. (withdrawn): A kit for diagnosing or predicting susceptibility to normal tension glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys).

20. (withdrawn): The kit of Claim 19, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

21. (withdrawn): A kit for diagnosing or predicting susceptibility to primary open angle glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

22. (withdrawn): The kit of claim 21, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

23. (withdrawn): A kit for diagnosing or predicting susceptibility to Leber's disease in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His).

24. (withdrawn): The kit of Claim 23, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

25. (withdrawn): An isolated polynucleotide consisting of a segment of SEQ ID NO:1,

wherein the segment comprises at least 90 contignuous nucleotides, and the at least 90 contignuous nucleotides includes position 9099 of the sequence, and wherein position 9099 of the sequence is A, or an isolated polynucleotide which is entirely complementary to the above segment.

26. (withdrawn): An isolated polynucleotide consisting of a segment of the sequence as shown in Claim 25, wherein the segment comprises at least 90 contignuous nucleotide, and the at least 90 contignuous nucleotide includes position 9101 of the sequence, and wherein position 9101 of the sequence is G, or an isolated polynucleotide which is entirely complementary to the above segment.

27. (withdrawn): An isolated polynucleotide consisting of a segment of SEQ ID NO:2,

wherein the segment comprises at least 90 contignuous nucleotides, and the at least 90 contignuous nucleotides includes codon 369, which is corresponding to the underlined nucleotides of the sequence, and wherein codon 369 is substituted such that it codes for Leu, or an isolated polynucleotide which is entirely complementary to the above segment.

28. (withdrawn): An isolated polynucleotide consisting of a segment of SEQ ID NO:3,

wherein the segment comprises at least 90 contignuous nucleotides, and the at least 90 contignuous nucleotides includes codon 144, which is corresponding to the underlined nucleotides of the sequence, and wherein codon 144 is substituted such that it codes for Gln, or an isolated polynucleotide which is entirely complementary to the above segment.

29. (withdrawn): A method for treating glaucoma in a patient who has an abnormality in the Myocilin gene, which comprises suppressing the expression of the abnormal Myocilin genes in the patient.

30. (withdrawn): The method of Claim 29, wherein the suppression is carried out by means of RNA interference method.

31. (withdrawn): A method for predicting the response of a subject to the treatment with a drug, which comprises the steps of; determining genotype in respect of at least one genetic polymorphism being associated with optic neuropathy, and predicting the response of the patient based on the genotype.

32. (withdrawn): The method of Claim 31, wherein the optic neuropathy is glaucoma or Leber's disease.

33. (withdrawn): The method of Claim 31, wherein the optic neuropathy is glaucoma.

34. (withdrawn): The method of Claim 31, wherein the at least one genetic polymorphism is 3123C>A polymorphism of the Angiotensin II type 2 receptor gene.

35. (withdrawn): The method of Claim 31, wherein the drug is an Angiotensin Receptor II antagonist.

36. (withdrawn): The method according to Claim 2, wherein the set of polymorphisms further comprises at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

37. (withdrawn): The method according to Claim 2, wherein the set of polymorphisms further comprises genetic polymorphisms selected from the group consisting of:

the combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene; and

the combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene.

38-39. (canceled).

40. (previously presented): The method according to Claim 2, wherein said open angle glaucoma is primary open angle glaucoma or normal tension glaucoma.

41. (previously presented): The method according to Claim 2, wherein said open angle glaucoma is primary open angle glaucoma.

42. (previously presented): The method according to Claim 2, wherein said open angle glaucoma is normal tension glaucoma.